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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
CROUCH, DEBORAH

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/465,596	SELDEN, RICHARD F.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *72-78,82-84 and 104-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-78,82-84 and 104-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 June 1995* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Inference numbers 104710, 104713 and 104714, relevant to the present prosecution, have been decided. Prosecution of the present application resumes. Claims 72-78, 82-84 and 104-108 are pending.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 72-78, 82-84 and 104-108 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 44 of copending Application No. 08/460,902. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claim 44 in '902.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA

sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claim 44 of '902 is drawn to a process for providing a human with a therapeutic protein comprising introducing human cells into a human, said human cells having been treated in vitro to insert therein a DNA segment encoding a therapeutic protein, said human

cells expressing in vivo in said human a therapeutically effective amount of said therapeutic protein.

As the '902 specification defines each term of claim 44 as encompassing the embodiments of present claims 72-78, 82-84 and 104-108, it would have been obvious to the ordinary artisan at the time of the instant invention to transfer a gene into a recipient given the method claim of '902.

Claims 72-78, 82-84 and 104-108 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 91-97, 99, 101-103, 106-108 and 129-131 of copending Application No. 08/461,292. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 91-97, 99, 101-103, 106-108 and 129-131 of '292.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human

cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 91-97, 99, 101-103, 106-108 and 129-131 of '292 are drawn to transfected, screened, cloned and expanded somatic cell preparations comprising transfected, cloned and expanded somatic cells stably expressing a DNA sequence obtained by transfecting somatic cell in vitro with the DNA sequence, screening the resulting transfected cells for a selected stably transfected with the DNA sequence and cloning and expanding the selected cells, wherein following injection into a recipient the cloned and expanded cell the DNA sequence is incapable of recombining with endogenous retroviral sequences and incapable of causing a chronic viral infection in the recipient patient; where the somatic cells are

human, a human clonal cell line, human primary cells, human immortalized cells, where the human somatic cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells; where the gene encodes a hormone, an enzyme or a receptor, where the gene encodes human growth hormone, human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, where the promoter is not of viral origin, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and a transfected, screened, cloned and expanded somatic cell preparation where the cells stably express a DNA sequence, where the preparation comprises a physiologically acceptable buffer and 10^5 to 10^{10} of the somatic cells, where the cells are obtained by transfecting somatic cells in vitro with the DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, expanding the selected cell to form the10^5 to 10^{10} cells and wherein following injection into a recipient, the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

The present specification defines and present claims 72-78, 82-84 and 104-108 requires using the cells of claims 91-97, 99, 101-103, 106-108 and 129-131 of '292. Therefore, at the time of the instant invention, it would have been obvious to arrive at the invention of present claims 72-78, 82-84 and 104-108 given the claims of '292.

Claims 72-78, 82-84 and 104-108 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 135-148 of copending Application No. 09/549,200. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 135-148 of '200.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation

properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 135-148 of '200 are drawn to methods producing a therapeutic product in a mammal comprising introducing into a mammal transfected primary or secondary cells comprising an exogenous nucleic acid molecule that comprises or is transcribed into a therapeutic product, the nucleic acid sequence being under control of exogenous nucleic acid sequences, wherein the method also includes culturing the secondary cells to form a clonal cell line, where in said cell a fibroblast, keratinocyte, epithelial cell, endothelial cell, glial cells, neural cells, blood cells, muscle cells or hepatocyte, where the therapeutic product is an enzyme, cytokine, hormone, antigen, antibody, clotting factor, regulatory protein, ribozyme, transcription protein, receptors or antisense nucleic acid molecules.

The present claims and the claims of '200 contain overlapping subject matter for an overlapping and obvious method. The present specification defines the cells to be administered to be a mixture of transfected and non-transfected cells. Therefore, at the time of the instant invention, it would have been obvious to arrive at the claimed methods given methods 135-148 of '200.

Claims 72-78, 82-84 and 104-108 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 65-68 of copending Application No. 09/549,697. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 135-148 of '200.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation

properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 65-68 of '697 are drawn to a method of producing a therapeutic product in a mammal comprising providing a DNA construct, transfecting primary or secondary cells with said construct, maintaining the transfected cells to allow homologous recombination, and introducing the cells into a mammal.

The present specification defines the DNA construct of the present claims to include a targeting construct so that the DNA sequence expressing a therapeutic product integrates into the genome. Further, the present claims encompass both integrated and episomal DNA constructs.

Thus, at the time of the present invention, it would have been obvious to the ordinary artisan to make the presently claimed method of transfer given the methods of producing a therapeutic product of claims 65-68 of '697.

These are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,303,379. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-21 in '379.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising

transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-21 of '379 are drawn to transfected primary or secondary cells comprising an exogenous nucleic acid molecule that comprises or is transcribed into a therapeutic product, where the cell is mammalian or human, where the cell comprises a selectable marker; transfected primary or secondary cells that stably expresses exogenous DNA sequence encoding a therapeutic product, the DNA sequence being under control of DNA sequence of non-retroviral origin, where in said cell a fibroblast, keratinocyte, epithelial cell, endothelial cell, glial cells, neural cells, blood cells, muscle cells or hepatocyte, where the therapeutic product is an enzyme, cytokine, hormone, antigen, antibody, clotting factor, regulatory protein, ribozyme, transcription protein; secondary eukaryotic cells transfected with an exogenous DNA sequence that encodes a therapeutic protein or is itself a therapeutic product, and a DNA sequence of non-retroviral origin that directs expression of the exogenous DNA sequence, where the DNA sequences are episomal, where the cell comprises a DNA sequence encoding a selectable marker, and where the cell is clonal; a heterogeneous cell strain having stably integrated into their genome an exogenous nucleic acid molecule that comprises or is transcribed into a therapeutic product, where the cell is

mammalian or human, where the cell comprises a selectable marker; transfected primary or secondary cells that stably expresses exogenous DNA sequence encoding a therapeutic product, the DNA sequence being under control of DNA sequences of non-retroviral origin, where in said cell a fibroblast, keratinocyte, epithelial cell, endothelial cell, glial cells, neural cells, blood cells, muscle cells or hepatocyte, where the therapeutic product is an enzyme, cytokine, hormone, antigen, antibody, clotting factor, regulatory protein, ribozyme, transcription protein; a heterogeneous cell stain of transfected primary or secondary cells that express exogenous DNA sequences encoding a therapeutic product where the DNA sequence is present episomally.

As each element of the methods in present claims 72-78, 82-84 and 104-108 is found with the cells of claims 1-21 of '379, and the '379 specification defines the cells as to be used in the presently claimed methods, it would have been obvious to the ordinary artisan at the time of present invention to arrive at the method of the present claims given the cells claimed in '379.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,048,729. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-11 in '729.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-11 of '729 are drawn to a clonal strain of secondary cells produced fro a transfected primary or secondary cell of primate origin which expresses a therapeutic protein, wherein the cells comprise an exogenous DNA sequence which encodes a therapeutic protein and an exogenous DNA sequence sufficient for expression of the DNA sequence encoding a therapeutic protein, where the secondary cells undergo about 20 or 27 doubling without being immortalized, where the cell is a transfected fibroblast, transfected keratinocyte, transfected epithelial cell, transfected endothelial cell, transfected glial cells, transfected neural cells, transfected blood cells, transfected muscle cells or transfected hepatocytes, where the cells is mammalian or human, where the therapeutic product is an enzyme, cytokine, hormone, antigen, antibody, clotting factor, regulatory protein, ribozyme, transcription protein, where the DNA encodes a selectable marker, and a method of using the clonal strain of secondary cells under conditions suitable for expression of the therapeutic protein.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,054,288. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-18 in '288.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-18 of '288 are drawn to methods of providing a therapeutic product in an effective amount in a mammal comprising transfecting primary cells with a DNA construct comprising exogenous DNA sequences encoding the therapeutic product and DNA sequences sufficient for expression of the exogenous DNA sequence, culturing the transfected primary cell to produce a clonal strain of secondary cells, expanding the clonal cells, and introducing a transfected secondary or a transfected clonal cell into a mammal to product an effective amount of the therapeutic produce, methods of providing a therapeutic product in an effective amount in a mammal comprising culturing primary cells to produce secondary cells, transfect the secondary cells with a DNA construct comprising exogenous DNA sequences encoding the therapeutic product and DNA sequences sufficient for expression of the exogenous DNA sequence, culturing the transfected secondary cells to produce a clonal strain of secondary cells, expanding the clonal cells, and introducing a transfected secondary cell into a mammal to product an effective amount of the therapeutic product where the primary cells are fibroblasts, keratinocytes, epithelial cells, endothelial cell, glial cells, neural cells, lymphocytes, bone marrow cells or hepatocyte, where the therapeutic product is an enzyme, a cytokine, a hormone, an antigen or a clotting factor, where the DNA sequences sufficient for expression are non-retroviral, and methods of providing a protein to a mammal at biologically significant levels comprising administering secondary transfected mammalian cells which express the protein at physiologically relevant levels, where the protein is an enzyme, a cytokine, a hormone, an antigen or a clotting factor, erythropoietin, human growth hormone or factor VIII.

The present specification defines the terms If claims 72-78, 82-84 and 104-108 as encompassing the elements of claims 1-18 of '288. As an example, while the present claims do not specifically claim the DNA sequence to encode Factor VIII, the specification defines "DNA sequence" as encompassing encoding factor VIII. Further, there is overlap of subject

matter in that the claims of '288 state the cells can be fibroblasts and that the DNA sequence encodes a hormone. Certain present claims state the same cell types, and states that the DNA sequence encodes insulin or growth hormone, both are hormones. Thus, it would have been obvious to the ordinary artisan at the time of the instant invention to make the method of present claims 72-78, 82-84 and 104-108 given claims 1-18 of '288.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,994,127. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-10 in '127.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin,

wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection,

electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-10 of '127 are drawn to an erythropoietin delivery system comprising transfected primary or secondary cells of a vertebrate which express erythropoietin upon introduction into a mammal, where the cells have an exogenous DNA sequence stably integrated into their genome and an exogenous DNA sequence sufficient for expression of the DNA sequence encoding erythropoietin, and a means for delivery of the cells, where the cells are fibroblasts, keratinocytes, epithelial cells, endothelial cells, glial cells, neural cells, blood cells, muscle cells or hepatocyte, where the cells are from a clonal strain, where the cells are a mixed population of two or more strains, where transfected cells are provided in an admixture with untransfected cells, where the cells are mammalian, wherein the cells also comprising exogenous DNA sequence encoding a selectable marker, where the cells do not contain erythropoietin in their non-transfected state, and where the cells are human.

The present claims either contain terms that are specifically identical to the terms of claims in '127, or the terms of the present specification are defined by the present specification as encompassing the terms of the claims in '127. For example, "DNA sequence" is defined by the present specification as encompassing erythropoietin, and the particular cell types are claimed in both sets of claims. Thus, at the time of the instant invention, it would have been obvious to the ordinary artisan to reach the methods presently claimed, given the erythropoietin delivery system of claims 1-10 in '127.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,048,524. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-9 in '524.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human

cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-9 of '524 are drawn to a method of expressing erythropoietin in a mammal comprising transfecting primary cells from a mammal, transfecting the cells with a DNA construct comprising an exogenous DNA sequence encoding erythropoietin and additional DNA sequences sufficient for expression of the DNA sequence encoding erythropoietin, culturing the transfected cells to product a clonal cell line and introduce the clonal transfected cells into a mammal of the same species as the primary cell donor mammal, where the cells are fibroblasts, keratinocytes, epithelial cells, endothelial cell, glial cells, neural cells, lymphocytes, bone marrow cells or hepatocyte, where the DNA sequences

sufficient for expression of the DNA sequence encoding erythropoietin are of non-viral or non-retroviral origin, and where the cells are administered in a barrier device that prevents a deleterious immune response.

The terms of the present claims are either the same as terms found in claims 1-9 of '524 or they are defined to encompass the claim language of claims 1-9 of 524. For example, both the present claims and 1-9 of '524 have language to the same type of primary cell, and the present specification defines "DNA sequence" as encompassing erythropoietin. Thus, at the time of the present invention, it would have been obvious to the ordinary artisan to make the presently claimed method, given claims 1-9 of '524.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 13-16 of U.S. Patent No. 6,187,305 B1. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-3 and 13-16 in '305.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of

recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-3 and 13-16 of '305 are drawn to a method of providing a therapeutic product in an effective amount comprising transfecting primary or secondary cells with a DNA construct comprising exogenous DNA sequences encoding a product to be expressed, DNA sequence homologous with genomic DNA sequences in the primary or secondary cell and DNA sequences encoding at least one selectable marker, maintaining primary or secondary cells under conditions appropriate for homologous recombination and introducing

primary or secondary cells having the homologous recombination into a mammal to produce an effective amount of therapeutic product, where the cells are fibroblasts, keratinocytes, epithelial cells, endothelial cell, glial cells, neural cells, lymphocytes, bone marrow cells or hepatocyte, where the primary cells are primary human cells, secondary human cells, primary mouse cells, secondary mouse cells, primary rabbit cells or secondary rabbit cells, where the therapeutic product is a hormone, where the hormone is growth hormone, where the hormone is erythropoietin, where the product is a clotting factor and where the clotting factor is factor VIII.

The present claims are obvious of claims 1-3 and 13-16 of '305 since both sets of claims have language to the same cell types, and the present specification defines "DNA sequence" as encompassing erythropoietin. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to arrive at the presently claimed method given the methods of claims 1-3 and 13-16 of '305.

Claims 72-78, 82-84 and 104-108 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,355,241 B1. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because each of the elements contained in present claims 72-78, 82-84 and 104-108 are contained within the elements of claims 1-16 in '241.

Present claims 72-78, 82-84 and 104-108 are drawn to a method of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence, screening transfected cells to select a cells that is stably transfected with the DNA sequence, cloning and expanding the selected cell in vitro and injected the resulting cell into the recipient subject, where, following injection, the DNA sequences is incapable of recombining with endogenous retroviral sequences and in capable of initiating chronic viral infection in the recipient subject, where the somatic cells are human cells, where the human cells are fibroblasts, myocytes, kidney capsular cells, endothelial cells, epithelial cells of the gut or pituitary cells, where the gene encodes human growth hormone or human insulin, wherein the transfection is by calcium phosphate-mediated transfection, microinjection, electroporation or DEAE-dextran transfection, a regulatable promoter, where the gene is a selectable gene and the promoter is operably linked to the selectable gene, where the selection comprises screening cells in vitro to select a cell possessing desired regulation properties; and methods of transferring a gene into a recipient subject comprising transfecting somatic cells in vitro with a DNA sequence comprising the gene and a promoter, where the somatic cells are stably transfected, screening resultant cells to select a cells by screening the cells by assaying for mRNA translation of the gene product, cloning and expanding the selected cell to form the10^5 to 10^{10} cells, combining the 10^5 to 10^{10} cells with a physiologically acceptable carrier and inject the cells into a recipient, wherein following injection the DNA sequence is incapable of recombining with endogenous retroviral sequences and the DNA sequence is incapable of causing a chronic viral infection in the recipient subject, where the gene encodes human growth hormone or insulin, where the DNA sequence integrated into the chromosome of the selected cell and where the DNA sequence replicates as an extrachromosomal plasmid.

Claims 1-16 of '241 are drawn to methods of producing erythropoietin in a mammal comprising transfecting primary cells with a nucleic acid construct comprising exogenous nucleic acid sequences encoding the therapeutic product and nucleic acid sequences sufficient for expression of the exogenous nucleic acid sequence, culturing the transfected primary cell to produce a clonal strain of secondary cells, expanding the clonal cells, and introducing a transfected secondary or a transfected clonal cell into a mammal to product an effective amount of the therapeutic produce, methods of providing a therapeutic product in an effective amount in a mammal comprising culturing primary cells to produce secondary cells, transfect the secondary cells with a nucleic acid construct comprising exogenous nucleic acid sequences encoding the therapeutic product and nucleic acid sequences sufficient for expression of the exogenous nucleic acid sequence, culturing the transfected secondary cells to produce a clonal strain of secondary cells, expanding the clonal cells, and introducing a transfected secondary cell into a mammal to product an effective amount of the therapeutic product where the primary cells are fibroblasts, keratinocytes, epithelial cells, endothelial cell, glial cells, neural cells, lymphocytes, bone marrow cells or hepatocyte, where the primary cells are human cells and where the erythropoietin is produced at levels sufficient to increase the hematocrit of the mammal.

The present claims are obvious of claims 1-16 of '241 since both sets of claims have language to the same cell types, and the present specification defines "DNA sequence" as encompassing erythropoietin. Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to arrive at the presently claimed method given the methods of claims 1-16 of '241.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 703-308-1126. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

dc
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